MINISTRY OF FOOD AND DRUG SAFETY
National Institute
of Food and Drug Safety Evalution

Safety assessment of Sweeteners

Food additives are substances that are intentionally used in the manufacture of food products. A typical food additive will ensure a technical effect (such as the maintenance or improvement of a product's quality), improve product characteristics (e.g., color), and/or preserve or enhance the nutritional characteristics of a product during its manufacture, processing, or preservation. Before food additives may be used in human food products, they must be assessed for safety and the absence of risks to public health must be verified. In addition, periodic reassessments of food additives are required, using surveys of those additives, after new safety information or new exposure estimates become available.

A sweetener is a food additive that imparts a sweet taste to food products. Sweeteners have been increasingly used after approval of sodium saccharin and D-sorbitol in 1962; currently 22 sweeteners are listed in the "Korea Food Additives Code". There are two kinds of sweeteners; natural and artificial sweeteners. Recently, Korean government announced policies to restrict the consumption of sugar, with the goal of preventing disease possibly related to excessive sugar intake. As a result, interest in artificial sweeteners with lower, or no, caloric content has increased. Simultaneously, scientific studies on the relationships between artificial sweeteners and fetal obesity have stirred public interest on potential adverse effects of artificial sweeteners.

The National Institute of Food and Drug Safety Evaluation (NIFDS) recently (2015–2016) performed safety reassessments on 16 of 22 sweeteners. Of the total, 6 sweeteners such as disodium glycyrrhizinate, erythritol, glycyrrhiza extract, neotame, enzymatically modified stevia glucosyl stevia, and D-xylose were not assessed because their usage is not significant or because additional toxicological information was not available. For each of the 16

sweeteners, the safety assessment was performed in four steps [(1) hazard identification, (2) hazard characterization, (3) exposure assessment, and (4) risk characterization] in accordance with the "Regulation on Risk Assessment Methods and Procedures" and the "Risk Assessment Guideline".

Unlike food contaminants, humans are exposed to food additives only through the consumption of processed food products. Therefore, for exposure assessments of food additives, estimated dietary intakes of food products containing a given additive are determined and the resulting calculated daily intakes are compared directly with each additive's acceptable daily intake (ADI, calculated on the basis of toxicological studies). In this manner the safety of a food additive is assessed.

Most countries adopt ADI values established by WHO/JECFA. However, the European Food Safety Authority (EFSA) and the US Food and Drug Administration establish their own ADIs for food additives. The NIFDS organized the Scientific Committee for Human Safety on Exposure (SCHSE) consisting of experts in medicine, toxicology, statistics and others, and assessed 16 sweeteners to determine their ADI values. Toxicological and epidemiological studies on each of the 16 sweeteners were reviewed to determine their potential effects on human health. These internationally recognized toxicological studies were reviewed with respect to acute, short-term, and chronic toxicity; carcinogenicity; genotoxicity; and reproductive/developmental toxicity. Based on the available information, the SCHSE evaluated the 16 sweeteners to determine an ADI for each. For any given food additive, if a threshold value was identified from toxicological studies in animals, numerical ADI values were assigned. In instances for which a threshold-based ADI was impossible to determine, owing to very low toxicological effects, "not specified" was proposed for the ADI, meaning that the committee found insufficient evidence to establish an ADI for the relevant food additives. Results of the ADI deliberations are summarized in Table 1.

ADI values of four artificial sweeteners, including sodium saccharin, were determined by the committee to be identical to those established by WHO/JECFA and EFSA. The ADI of acesulfame potassium was also found to be identical to that of EFSA, but lower than that of WHO/JECFA. When results from the two-year long-term carcinogenicity studies in rats and beagles were reviewed, beagles exhibited some toxicological responses to acesulfame potassium. Accordingly, 900 mg/kg bw/day in beagles was selected as a no observable effect level (NOEL) and an uncertainty factor of 100 was applied to establish an ADI of 9 mg/kg bw/day for acesulfame potassium.

Table 1. Acceptable daily intake (ADI) of 16 sweeteners

Sweetener	ADI (mg/kg bw/day)
Sodium saccharin	0 – 5
Sucralose	0 – 15
Acesulfame potassium	0 – 9
Aspartame	0 – 40
Steviol glycosides	0 – 4
Lactitol	Not specified
D-ribose	Not specified
D-mannitol	Not specified
D-maltitol	Not specified
Maltitol syrup	Not specified
Isomalt	Not specified
D-sorbitol	Not specified
D-sorbitol solution	Not specified
Xylitol	Not specified
Thaumatin	Not specified
Polyglycitol syrup	Not specified

For the conduct of the exposure assessments, four sweeteners (sodium saccharin, sucralose, aspartame, and acesulfame potassium) were selected. These molecules were selected based on the availability of appropriate test methods for their quantitative determination in food products and because each had an established ADI. The content of each additive in food products distributed throughout Korea was analyzed and actual intake levels for each additive were estimated by consumer age. After conduct of market surveys and detailed review of documents such as manufacturing reports and import declarations, data on sweetener use were compiled. Sample products were then purchased from department stores, large-scale discount stores, convenience stores and traditional markets located in major cities, including Seoul, Busan, Daegu, Daejeon and Gwangju, as well as from internet-based retailors. A total of 906 products representing 30 food categories of established and standard use were collected. Purchased sample products were used for the quantitative determination of the sweeteners using liquid chromatography. When a test result for a given analyte in a test sample was below the method detection limit, the data point was treated as a "0" and reported as not detected (ND). Relatively high concentrations of sweeteners found in products are summarized as follows. Mean sodium saccharin content was 543.5 μg/g for spiced/seasoned jeot[1], 200 μg/g for pickled food[2] and 35.8 μg/g for kimchies. Mean sucralose content was 130.9 μg/g for chewing gum, 29.4 μg/g for ice candy and 18.1 μg/g for mixed beverages[3]. Mean acesulfame potassium content was 305.7 μg/g for chewing gum, 56.3 μg/g for beverage base[4] and 44.5 μg/g for spiced/seasoned jeot. Mean aspartame content was 269.2

[1] Jeot refers to a liquid product manufactured by being separated from salted and fermented seafood

[2] Picked food refers to a product made by salting main ingredients with salt, soy sauce or vinegar or mixing them and then treating them with spices. It includes salt-pickled food, soy sauce-pickled food, or vinegar-pickled food etc.

[3] Mixed beverage refers to a drink processed by adding foods or additives to drinking water

[4] Beverage base refers to a product processed by using animal/vegetable substances, or after then, adding foods or additives to drink it by mixing with water

μg/g for processed cocoa products, 146.5 μg/g for beverage base and 74.5 μg/g for candy.

Estimated daily intakes (EDIs) of the four sweeteners were calculated using food-consumption data for the Korean population derived from the 2010–2013 Korea National Health and Nutrition Examination Survey (KNHANES) and the quantitative results of sweeteners in the assayed food samples. Mean food consumption was based on matching of actual analyzed products and food consumption data for the Korean population (using the 1st code from KNHANES database). In addition, mean body weight (kg) of all persons participated in KNHANES was used in establishing exposures on a body weight basis. For example, EDI was calculated for the total population and for high-consumption groups (by age and gender), according to the following equation:

$$EDI_p \text{ (mg/kg bw/day)} = \sum (C_i \times F_i)/W_p$$

where EDI_p is the daily intake of sweetener for person *p*; C_i is the mean concentration of sweetener in each food class (mg/kg); F_i is the individual daily consumption of each food class (g/day); and W_p is body weight of the general Korean population or specific consumer subgroup (kg).

For the 12 sweeteners, such as lactitol, for which appropriate analytical methods do not exist for food products, the “poundage method” was used to calculate daily intake per capita:

$$\text{Daily intake per capita (mg/person/day)} = \frac{\text{Production amount (kg) + Import amount (kg) - Export amount (kg)} \times 10^6 \text{ mg/kg}}{\text{Total population} \times 365 \text{ (days)}}$$

The poundage method is based on mean values for total production, total import, and total export of a food product during the past 3 years (2012–2014). These statistical data were available in "Report of Food and Food Additives Production" and "Annual Report of Imported Food Test" published by the Ministry of Food and Drug Safety. The EDIs of the 16 sweeteners evaluated by the SCHSE are summarized in Table 2. The poundage method employed in this safety assessment is the most convenient and economical method to evaluate consumption of food additives on the basis of supplies of food additives. This method assumes that food additives are uniformly consumed within the population of an area where the food additives are manufactured or imported. Therefore, the poundage method does not accurately reflect actual consumption levels by groups or subgroups of people. Further, because food additives are sold and distributed in many forms (as various products, in mixed preparations, either as final products or in "premixes" used to prepare final products), it is extremely difficult to accurately assess actual human exposures using the poundage method. In order to overcome problems associated with the poundage method, actual analysis of sweeteners in food products under distribution is the most accurate way to calculate EDI.

Unlike contaminants, sweeteners are purposely added as food additives and they are largely consumed in processed foods. Therefore, EDIs were compared with ADIs to investigate the likelihood of potentially hazardous effects in humans. The safety level evaluated by comparing EDI with ADI was 3.6% for sodium saccharin, 2.1% for sucralose, 2.9% for acesulfame potassium, 0.8% for aspartame and 4.3% for steviol glycosides. In addition, no hazardous effects were expected for 11 sweeteners, including lactitol.

This safety assessment report was scientifically reviewed by the SCHSE of NIFDS and commented by professional members. When new information is obtained in the future, safety assessment will be conducted again. This report can be found at the NIFDS website.

Table 2. Results of estimated daily intake (EDI) and the safety assessment of 16 sweeteners.

Name	Evaluation method	EDI (mg/kg bw/day)	Safety assessment
Sodium saccharin	Consumption evaluation	0.18	3.6% of ADI, safe
Sucralose	Consumption evaluation	0.32	2.1% of ADI, safe
Acesulfame potassium	Consumption evaluation	0.26	2.9% of ADI, safe
Aspartame	Consumption evaluation	0.33	0.8% of ADI, safe
Steviol glycosides	Poundage method	0.17	4.3% of ADI, safe
Lactitol	Poundage method	0.03	No hazardous effect expected
D-ribose	Poundage method	0.0021	No hazardous effect expected
D-mannitol	Poundage method	0.16	No hazardous effect expected
D-maltitol	Poundage method	0.84	No hazardous effect expected
Maltitol syrup	Poundage method	6.25	No hazardous effect expected
Isomalt	Poundage method	0.40	No hazardous effect expected
D-sorbitol	Poundage method	13.44	No hazardous effect expected
D-sorbitol solution	Poundage method	17.65	No hazardous effect expected
Xylitol	Poundage method	4.15	No hazardous effect expected
Thaumatin	Poundage method	0.000085	No hazardous effect expected
Polyglycitol syrup	Poundage method	1.73	No hazardous effect expected

Key words: Food additive, Sweetener, Acceptable daily intake, Safety assessment